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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/650,412
Filing Date: August 28, 2003
Appellant(s): THOMAS ET AL.

Melissa W. Acosta
(Reg. No. 45,872)
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 4/26/2007 appealing from the Office action mailed 5/17/2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is substantially correct. Note the independent claim is claim 22 rather than claim 20 (See page 4, line 14, of the Appeal Brief filed 4/26/2007).

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

US 6,143,247	SHEPPARD, JR. ET AL.	11-2000
US 6,319,469	MIAN ET AL.	11-2001
US 5,660,993	CATHEY ET AL.	08-1997
US 5,800,778	CHEN ET AL.	09-1998
US 5,190,879	WOLFE ET AL.	03-1993
WO 94/26413	COOK	11-1994

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

A. Claims 22-25 and 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheppard, Jr. et al.(US 6,143,247) in view of Mian et al.(US 6,319,469) and Cathey et al.(US 5,660,993).

The reference of Sheppard, Jr. et al. discloses an assay device and method of use which includes a disc device that includes a plurality of micro-channel elements (shown in Figure 2). Each element includes a cell growth chamber (24) which allows cells to be introduced and cultured for attachment (See column 4, lines 14-17). The reference discloses detection of test compounds on the cultured cells (See column 7, lines 13-32 and Example 3).

Claim 22 first differs by reciting specific construction limitations such as the use of multiple micro-channel elements and cover limitations.

The reference of Sheppard, Jr. et al. discloses that the device as disclosed by Mian et al. can be used to construct the system of Sheppard, Jr. et al. (See column 3, lines 28-38 which makes reference to Application 08/768,990 in the specification of Sheppard, Jr. et al.).

The reference of Mian et al. discloses a base and cover construction for forming a plurality of micro-channel elements (See Figure 1B and Example 1, column 39, line 21, to column 40, line 5).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ the construction techniques of Mian et al. to construct the device of Sheppard, Jr. et al. for the known and expected result of providing a device as is required of the Sheppard, Jr. et al. reference.

Claim 22 further differs by reciting that the device includes "a hydrophobic barrier or valve in at least one of said chambers or said channels" "wherein said valve comprises a localized region of hydrophobicity within said chamber or said channel".

The references of Sheppard, Jr. et al. and Mian et al. disclose that the use of valves to control the flow of liquid between the chambers of the device is known (See column 13, lines 1-9; column 13, line 65, to column 14, line 30; and column 20, lines 12-67, of the reference of Sheppard, Jr. et al.). The list of disclosed valves includes capillary microvalves wherein the fluid flow is stopped based on the geometry of the channel and surface properties of the substrate material and fluid.

The reference of Cathey et al. discloses that it is known in the art to control the flow of liquids between the chambers or channels of a capillary flow device by using capillary valves or "hydrophobic areas in that particular region" in which one wishes to slow or impede fluid flow through a particular region of the channel (See column 5, lines 47-60). The reference of Cathey et al. establishes that a capillary valve and localized region of hydrophobicity are art recognized equivalents for enhancing or controlling the flow of fluids through an assay device.

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a hydrophobic region or localized region of hydrophobicity within the device of the device of the reference of Sheppard, Jr. et al. for the predictable result of providing an alternative means recognized in the art to achieve the same result, control the flow of fluid between the chambers as is suggested and required of the reference of Sheppard, Jr. et al.

With respect to claims 23 and 24, the reference of Sheppard, Jr. et al. discloses that a suspension of cells can be attached in the cell chambers (See column 4, lines 1-17).

With respect to claim 25, the device suggested by the combination of the references of Sheppard, Jr. et al. and Mian et al. would be a rotatable disc with a center inlet port and annular sample chamber. Note the reference of Sheppard, Jr. et al. discloses that the device can be a rotatable disc (See column 3, lines 28-33 of Sheppard, Jr. et al.) with a sample introduction port and an annular sample reservoir (element 21, Figure 2 of Sheppard, Jr. et al.). Note that sample reservoir (21) is annularly positioned on the disc as shown in Figure 2.

With respect to claim 33, the reference of Sheppard, Jr. et al. discloses the use of three-dimensional surfaces for the cell accumulation chamber (See column 16, lines 38-42). With

respect to the use of beads or pillars for cell attachment, the use of surface area extending surfaces in cell culture is well known in the art for the known and expected result of increasing the surface area of attachment for the cells to attach and thus increasing the number of cells which can be maintained within the cell culture chamber (24).

With respect to the use of inlet channels of one size verses an outlet of a smaller size of claims 34 and 35, the reference of Mian et al. discloses that it is known in the art to control the flow of liquid through a plurality of zones using changes in cross-sectional area between the zones (See column 19, lines 25-63).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to provide differences in cross-section between the inlet and outlet of the culture chamber and other chamber for the known and expected result of controlling the flow of liquid between the difference chambers.

Additionally, the reference of Sheppard, Jr. et al. also discloses constructing the cell accumulation chambers such that cells entering the chamber are prevented from being removed from the chamber by fluids flowing into the chamber (See column 26, lines 20-30).

Again, this would suggest to one of ordinary skill in the art to provide an outlet channel in the accumulation chamber that is less than the diameter of the cells or beads retained within the accumulation chamber.

With respect to claims 36-38, the claims differ by reciting the use of additional detection chambers for detecting metabolites released by the cell culture.

The reference of Sheppard, Jr. et al. discloses that cells captured or retained within the accumulation chamber can be analyzed within the chamber or eluted and transferred to a

collection chamber (See column 18, lines 31-65). Also note that the reference of Sheppard, Jr. et al. discloses the use of serially connected chambers (See Figures 3 and 4) for a number of reasons that would have been well within the purview of one having ordinary skill in the art.

As a result, one of ordinary skill in the art would have recognized that the accumulation chamber can be communicated with additional chambers used in the detection process as suggested by the references of Sheppard, Jr. et al. and Mian et al. for the known and expected result of providing an alternative means recognized in the art to achieve the same result, detection of metabolites produced by the cultured cells in response to treatment agents exposed to the cells.

B. Claims 21, 26 and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheppard, Jr. et al.(US 6,143,247) in view of Mian et al.(US 6,319,469) and Cathey et al.(US 5,660,993) taken further in view of Chen et al.(US 5,800,778).

The combination of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. has been discussed above.

Claims 21 and 26 further differ by reciting that one or more components (the cover) of the device are constructed of a gas permeable plastic material.

The reference of Chen et al. discloses that it is known in the art to employ a gas permeable cover in a test device which is constructed with a base including channels and chambers with the gas permeable cover. The reference discloses that the use of the cover provides increased growth rates from an enhanced oxygen environment (See column 3, lines 6-7).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the device of the primary reference with a gas permeable cover member for the known and expected advantages disclosed by the reference of Chen et al.

With respect to the cell attachment means of claim 21, the reference of Sheppard, Jr. et al. discloses the use of non-specific cell adhesion coating (See column 4, lines 1-17).

With respect to the specifics of the cell attachment means of claims 29-31, the reference of Sheppard, Jr. et al. discloses the use of chemical surface treatments or the use of adhesion proteins (See column 16, lines 1-37). The specific adhesion protein employed would have been well within the purview of one having ordinary skill in the art using well known proteins such as collagen or fibronectin.

With respect to claim 32, the reference of Sheppard, Jr. et al. discloses the use of three-dimensional surfaces for the cell accumulation chamber (See column 16, lines 38-42). With respect to the use of beads or pillars for cell attachment, the use of surface area extending surfaces in cell culture is well known in the art for the known and expected result of increasing the surface area of attachment for the cells to attach and thus increasing the number of cells which can be maintained within the cell culture chamber (24).

C. Claims 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheppard, Jr. et al.(US 6,143,247) in view of Mian et al.(US 6,19,469); Cathey et al.(US 5,660,993) and Chen et al.(US 5,800,778) taken further in view of Wolfe et al.(US 5,190,879).

The combination of the references of Sheppard, Jr. et al., Mian et al., Cathey et al. and Chen et al. has been discussed above.

While the combination of the references Sheppard, Jr. et al., Mian et al., Cathey et al. and Chen et al. suggest the use of a gas permeable cover, the above claims recite specific materials for the gas permeable material.

The reference of Wolfe et al. provides a list known materials which can be used as a gas permeable material in a culture device (See column 2, lines 39-68).

In view of this teaching and in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ any of the known gas permeable materials as the cover member for the known and expected result of providing an alternative means recognized in the art to achieve the same result, provide gas exchange to a culture chamber.

D. Claims 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheppard, Jr. et al.(US 6,143,247) in view of Mian et al.(US 6,319,469) and Cathey et al.(US 5,660,993) taken further in view of Cook (WO 94.26413).

The combination of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. has been discussed above.

While the reference of Sheppard, Jr. et al. discloses the use of optically detectable labels within the chambers (See column 3, lines 39-67), Claims 39 and 40 differ by reciting that the device includes a layer of a scintillant substance and includes a binding moiety.

The reference of Cook discloses that it is conventional in the art to study of the interaction of biological molecules with cultured cells using a layer of a scintillant substance and a binding moiety (See pages 9-17).

In view of this teaching, in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to employ the scintillation assay technique disclosed by the reference of Cook in the system of the modified primary reference of Sheppard, Jr. et al. for the known and expected result of providing an art recognized means for observing cellular processes with respect to a reagent as is performed in the system of the modified primary reference.

(10) Response to Argument

A. Rejection under 35 U.S.C. 103(a) as being unpatentable over Sheppard, Jr. et al.(US 6,143,247) in view of Mian et al.(US 6,319,469) and Cathey et al.(US 5,660,993).

1. Claims 22-24 and 33

Argument (a)(i):

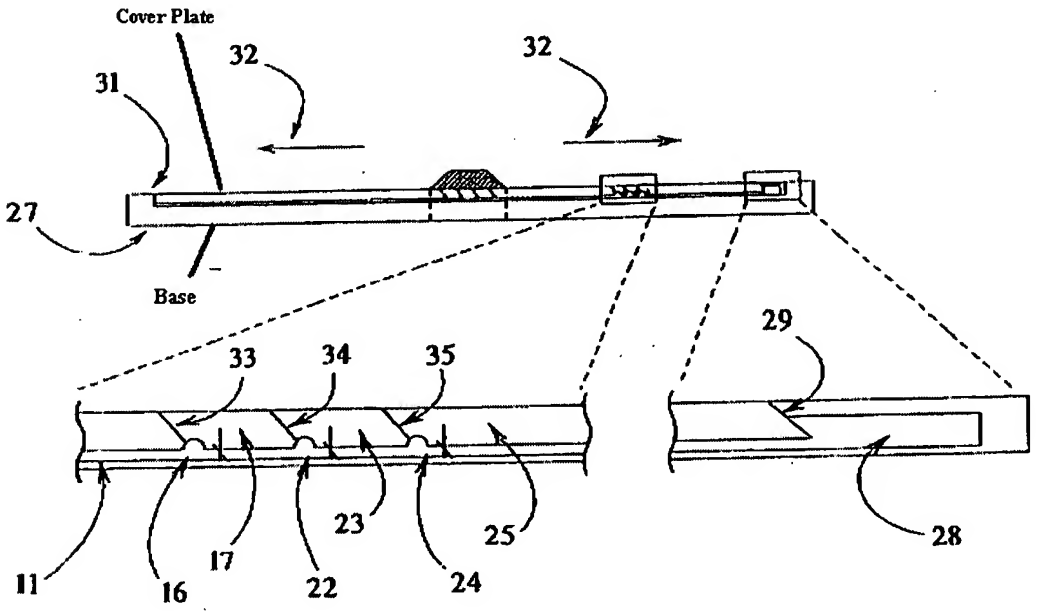
Appellants argue (See pages 6-8 of the Appeal Brief filed 4/26/2007) that the references of Sheppard, Jr. et al. and Mian et al. fail to disclose the cover plate or hydrophobic valve elements required of independent claim 22.

With respect to the claimed cover plate, Appellants stress that Figure 1B of Mian et al. and its related disclosure fail to disclose a cover plate and the Patent Office provides no guidance on how Figure 1B supplies the cover plate limitation. Appellants further state "Figure 1B shows

a contiguous microfluidic structure with air vent 29 creating the superficial appearance of a two piece device in the cross sectional image".

In response, the Examiner maintains that Figure 1B discloses a microfluidic device that includes a base layer and cover plate as shown below:

FIG. 1B



It is noted that the disclosure of Mian et al. does not identify elements 27 or 31 in Figure 1B and does not identify a base layer or plate and/or a cover layer or plate. However, the Examiner maintains that the use of base and cover layers or plates when constructing microfluidic devices is notoriously well known in the art and that one of ordinary skill in the art when reviewing Figure 1B would clearly recognize that the device of Figure 1B is constructed

using a base layer or plate and cover layer or plate. To further support this position, the Examiner points to Example 1 of Mian et al. (See column 39, line 21, to column 40, line 8, especially column 40, lines 2-3) which discloses the fabrication technique used to make a microfluidic device, such as in Figure 1B, and includes a step of providing a top layer comprising access ports and air vents, ports or shafts.

With respect to the claimed hydrophobic valve, Appellants stress that the capillary valves disclosed in the references of Sheppard, Jr. et al. and Mian et al. are structurally and mechanically unrelated to the claimed hydrophobic valves.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the Examiner has relied upon the disclose of Cathey et al. to address the structure of the claimed hydrophobic valve and the combination of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. meet the claimed structure for the reasons set forth in the rejection of claim 22.

Argument (a)(ii):

Appellants argue (See pages 8-9 of the Appeal Brief filed 4/26/2007) that the reference of Cathey et al. fails to disclose the cover plate or hydrophobic valve elements required of independent claim 22. Appellants recognize that the Patent Office has not relied upon the reference of Cathey et al. to address the claimed cover plate. Appellants stress that the cited portion of the reference of Cathey et al. does not supply the claimed hydrophobic valve element

because the disclosure of hydrophobic areas is only related to rate control where flow is enhanced or slowed and/or flow is directed. Appellants are of the position the reference of Cathey et al. does not disclose a hydrophobic valve because the only disclosure of valving is related to the disclosed capillary valve while the hydrophobic areas are only disclosed as slowing the flow.

In response, the Examiner is of the position that the reference of Cathey et al. teaches a hydrophobic valve for the following reasons. Claim 22 defines the claimed hydrophobic valve as "a localized region of hydrophobicity within said chamber or said channel". The reference of Cathey et al. discloses that it is known to provide localized hydrophobic areas in a microfluidic device where one wishes to slow or impede fluid flow through a particular region of the channel (See column 5, lines 53-55). As a result, the hydrophobic valve of claim 22 is considered to be structurally and functionally the same as the hydrophobic area disclosed by the reference of Cathey et al.

Argument (b)(i):

Appellants argue (See pages 9-10 of the Appeal Brief filed 4/26/2007) that the use of a hydrophobic valve in the devices of Sheppard, Jr. et al. and Mian et al. is not obvious in view of the disclosures of these references. Appellants stress that while the inventor of Sheppard, Jr. et al. and Mian et al. provide a list of valves and are of ordinary skill in the art, the list fails to include hydrophobic valves. Appellants also argue that the Patent Office has employed improper hindsight by modifying the references of Sheppard, Jr. et al. and Mian et al. to include a hydrophobic valve.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, while the references of Sheppard, Jr. et al. and Mian et al. are silent as to the use of hydrophobic valves, the references clearly disclose the use of capillary valves. The reference of Cathey et al. was relied upon by the Examiner as a teaching that capillary valves are functionally equivalent to hydrophobic valves or area within a microfluidic device. As a result, it is the combination of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. that address the obviousness of the hydrophobic valve. The Examiner was not relying solely on the disclosures of the references of Sheppard, Jr. et al. and Mian et al.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As stated immediately above, the Examiner is of the position that the combined teachings of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. suggest the use of a hydrophobic valve or region within a microfluidic device which meets the limitations of claim 22.

Appellants additionally argue that the reference of Sheppard, Jr. et al. teaches against the use of hydrophobic surfaces as valves because the reference discloses the use of hydrophobic surfaces for promoting sample material adsorption. Appellants conclude that use of hydrophobic surfaces, other than for promoting sample material adsorption, would run contrary to the teachings in Sheppard, Jr. et al. and the intended purposes of the Sheppard, Jr. et al. devices.

In response, Appellants' comments are not found to be persuasive because the discussion in Sheppard, Jr. et al. of the hydrophobic areas is mainly concerned with the chambers for cell accumulation and/or detection. The valve structures for controlling the flow of fluid in the device are positioned within the microchannels connecting the chambers of the device (See Figures 3 and 4 of Sheppard et al.). As a result, the disclosure of Sheppard is not considered to teach away from the use and/or preclude the use of hydrophobic valves within the microfluidic device for controlling the flow of fluid between the chambers within the device.

Argument (b)(ii):

Appellants argue (See page 10 of the Appeal Brief filed 4/26/2007) that the reference of Cathey et al. does not disclose hydrophobic valves of the instant claims. Appellants stress that the capillary valves actually used by the reference of Cathey et al. are unrelated in structure or mechanism of function to the claimed hydrophobic valves. Appellants further argue that the Patent Office has employed impermissible hindsight by erroneously reading into the prior art the hydrophobic valve element.

As stated in the response to argument (a)(ii) above, the Examiner is of the position that the reference of Cathey et al. teaches a hydrophobic valve for the following reasons. Claim 22

defines the claimed hydrophobic valve as "a localized region of hydrophobicity within said chamber or said channel". The reference of Cathey et al. discloses that it is known to provide localized hydrophobic areas in a microfluidic device where one wishes to slow or impede fluid flow through a particular region of the channel (See column 5, lines 53-55). As a result, the hydrophobic valve of claim 22 is considered to be the same as the hydrophobic area disclosed by the reference of Cathey et al.

Additionally, while the capillary valves of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. may be structurally different from the hydrophobic valve or region of claim 22 and hydrophobic area of Cathey et al., the Examiner is of the position that the capillary valves and hydrophobic region or area are functional equivalents in view of the disclosure of Cathey et al. which conveys to one of ordinary skill in the art that hydrophobic areas can be used as an alternative to capillary valves to achieve the predictable result of controlling the flow of fluid within a microfluidic device.

As stated in the response to argument (b)(i) above, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As stated previously, the Examiner is of the position that the combined teachings of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. suggest the use of a hydrophobic valve or region within a microfluidic device meeting the limitations of claim 22.

Argument (c)(i):

Appellants argue (See page 11 of the Appeal Brief filed 4/26/2007) that since the Patent Office has not identified all of the elements (i.e., cover plate and hydrophobic valve) of claim 22, "it is impossible for the Patent Office to articulate a valid motivation to combine these unaccounted for elements".

In response, for reasons previously discussed in response to arguments (a)(i) and (a)(ii) above, the Examiner is of the position that the combination of the prior art references of Sheppard, Jr. et al., Mian et al. and Cathey et al. disclose all of the elements recited in claim 22, especially the claimed cover plate and hydrophobic valve.

Argument (c)(i)(1):

Appellants argue (See pages 11-12 of the Appeal Brief filed 4/26/2007) that even if the reference of Cathey et al. discloses hydrophobic valves, the reference of Cathey et al. does not support the position that the art recognizes hydrophobic valves as equivalents to capillary valves. Appellants stress that the reference of Cathey et al. does not disclose a reduction to practice of hydrophobic valves and does not reference other prior art that actually uses hydrophobic valves.

In response, Applicants' comments are not found to be persuasive for the following reasons. First, the Examiner maintains that one of ordinary skill in the art in view of the disclosure of Cathey et al. (column 5, lines 47-60) would recognize the hydrophobic regions to be a functional equivalent to a capillary valve. One of ordinary skill in the art would recognize that a hydrophobic material positioned within a capillary channel of the device of Cathey et al.

would impede or stop the flow of liquid within the channel based merely on the driving pressures applied to the sample liquid. As with the capillary valve, above a certain driving pressure there is flow and below there is no flow. Additionally, while the capillary valves of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. may be structurally different from the hydrophobic valve or region of claim 22 and hydrophobic area of Cathey et al., the Examiner is of the position that the capillary valves and hydrophobic region or area are functional equivalents in view of the disclosure of Cathey et al. which conveys to one of ordinary skill in the art that hydrophobic areas can be used as an alternative to capillary valves to achieve the predictable result of controlling the flow of fluid within a microfluidic device.

Argument (c)(i)(2) and (c)(i)(3):

Appellants once again argue (See page 12 of the Appeal Brief filed 4/26/2007) that the reference of Sheppard, Jr. et al. teaches against the use of hydrophobic surfaces as valves because the reference discloses the use of hydrophobic surfaces for promoting sample material adsorption. Appellants conclude that use of hydrophobic surfaces, other than for promoting sample material adsorption, would run contrary to the teachings in Sheppard, Jr. et al. and the intended purposes of the Sheppard, Jr. et al. devices.

In response, Appellants' comments are not found to be persuasive because the discussion in Sheppard, Jr. et al. of the hydrophobic areas is mainly concerned with the chambers for cell accumulation and/or detection. The valve structures for controlling the flow of fluid in the device are positioned within the microchannels connecting the chambers of the device (See Figures 3 and 4 of Sheppard, Jr. et al.). As a result, the disclosure of Sheppard, Jr. et al. is not

considered to teach away from the use and/or preclude the use of hydrophobic valves within the microfluidic device for controlling the flow of fluid between the chambers within the device.

2. Claim 25

Appellants argue (See page 13 of the Appeal Brief filed 4/26/2007) that the references of Sheppard, Jr. et al. and Mian et al. do not disclose or suggest an annular sample chamber.

In response, the Examiner is of the position that the reference of Sheppard, Jr. et al. discloses that the device can be a rotatable disc (See column 3, lines 28-33 of Sheppard, Jr. et al.) with a sample introduction port and an annular sample reservoir (element 21, Figure 2 of Sheppard, Jr. et al.). Note that sample reservoir (21) is annularly positioned on the disc as shown in Figure 2.

3. Claims 34-35

Appellants argue (See pages 13-14 of the Appeal Brief filed 4/26/2007) that the passage of Mian et al. has nothing to do with the limitations of claims 34-35.

In response, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). In this case, the references of Sheppard, Jr. et al. and Mian et al. both suggest controlling or altering the cross-sectional dimensions within the device for controlling the flow of fluid within the device (See column 20, lines 32-64, of Sheppard, Jr. et al. and column 19, lines 25-63 of Mian et al.). Additionally, the reference of Sheppard, Jr. et al. also

discloses constructing the cell accumulation chambers such that cells entering the chamber are prevented from being removed from the chamber by fluids flowing into the chamber (See column 26, lines 20-30). Again, this would suggest to one of ordinary skill in the art to provide an outlet channel in the accumulation chamber that is less than the diameter of the cells or beads retained within the accumulation chamber.

4. Claims 36-38

Appellants argue (See page 14 of the Appeal Brief filed 4/26/2007) that the rejection of claims 36-38 lacks substantial evidence to support the conclusion that the claimed subject matter is obvious.

In response, claim 36 requires that the device include "one or more assay chambers for performing assays involving cellular constituents and connected in line between said cell growth chamber and said outlet channel". The reference of Sheppard, Jr. et al. discloses that cells captured or retained within the accumulation chamber can be analyzed within the chamber or eluted and transferred to a collection chamber (See column 18, lines 31-65). As a result, one of ordinary skill in the art would have recognized that the accumulation chamber can be communicated with additional chambers used in the detection process as suggested by the references of Sheppard, Jr. et al. and Mian et al. Also note that the reference of Sheppard, Jr. et al. discloses the use of serially connected chambers (See Figures 3 and 4) for a number of reasons that would have been well within the purview of one having ordinary skill in the art.

With respect to claims 37 and 38, as discussed previously, the references of Sheppard, Jr. et al. and Mian et al. both suggest controlling or altering the cross-sectional dimensions within

the device for controlling the flow of fluid within the device (See column 20, lines 32-64, of Sheppard, Jr. et al. and column 19, lines 25-63 of Mian et al.). Additionally, the reference of Sheppard, Jr. et al. also discloses constructing the cell accumulation chambers such that cells entering the chamber are prevented from being removed from the chamber by fluids flowing into the chamber (See column 26, lines 20-30). Again, this would suggest to one of ordinary skill in the art to provide an outlet channel in the accumulation chamber that is less than the diameter of the cells or beads retained within the accumulation chamber.

B. Rejection under 35 U.S.C. 103(a) as being unpatentable over Sheppard, Jr. et al.(US 6,143,247) in view of Mian et al.(US 6,319,469) and Cathey et al.(US 5,660,993) taken further in view of Chen et al.(US 5,800,778).

With respect to claims 21, 26 and 29-32, Appellants argue (See page 14 of the Appeal Brief filed 4/26/2007) that the rejection is improper for the same reasons as set forth previously with respect to claim 22.

In response, the Examiner maintains that the combination of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. is proper for the reasons already set forth in the responses to argument A above.

C. Rejection under 35 U.S.C. 103(a) as being unpatentable over Sheppard, Jr. et al.(US 6,143,247) in view of Mian et al.(US 6,19,469); Cathey et al.(US 5,660,993) and Chen et al.(US 5,800,778) taken further in view of Wolfe et al.(US 5,190,879).

With respect to claims 27 and 28, Appellants argue (See page 14 of the Appeal Brief filed 4/26/2007) that the rejection is improper for the same reasons as set forth previously with respect to claim 22.

In response, the Examiner maintains that the combination of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. is proper for the reasons already set forth in the responses to argument A above.

D. Rejection under 35 U.S.C. 103(a) as being unpatentable over Sheppard, Jr. et al.(US 6,143,247) in view of Mian et al.(US 6,319,469) and Cathey et al.(US 5,660,993) taken further in view of Cook (WO 94.26413).

1. Claim 39:

With respect to claim 39, Appellants argue (See page 15 of the Appeal Brief filed 4/26/2007) that the rejection is improper for the same reasons as set forth previously with respect to claim 22.

In response, the Examiner maintains that the combination of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. is proper for the reasons already set forth in the responses to argument A above.

2. Claim 40:

With respect to claim 40, Appellants argue (See page 15 of the Appeal Brief filed 4/26/2007) that the rejection is improper for the same reasons as set forth previously with respect to claim 22.

In response, the Examiner maintains that the combination of the references of Sheppard, Jr. et al., Mian et al. and Cathey et al. is proper for the reasons already set forth in the responses to argument A above.

Appellants also argue that the combination further including the reference of Cook is improper because the disclosure of Cook "has nothing to do with the additional limitation in claim 40 directed to platform attached, non-cellular binding moieties".

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, it is the combination of the teachings of Sheppard, Jr. et al., Mian et al., Cathey et al. and Cook that result in a structure that meets the limitations of claim 40.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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